DETAILED ACTION

RESPONSE TO AMENDMENT

Status of Application/Amendments/claims

1. Applicant's amendment filed 3/1/10 is acknowledged. Claims 2-4, 16-18, 20-28, 36-50, 53 and 58 are cancelled. Claims 1, 5, 6, 9, 29-30, 34-35, 54, 59 and 63 are amended. Claim 74 is newly added. Claims 1, 5-15, 19, 29-35, 51-52, 54-57, 59-73 and new claim 74 are pending in this application and are under examination with respect to IFN-1α/β in this office action.

2. Applicant's arguments filed on 3/1/10 have been fully considered but they are not deemed to be persuasive for the reasons set forth below.

Claim Rejections/Objections Withdrawn

3. The objection to claim 4 is moot because the claim is canceled.

The rejection of claims 1, 4-15, 19, 29-36 and 50-73 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in response to Applicant's amendment and arguments on p. 15-16.

The rejection of claims 1, 4-15, 19 and 29- under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement due to new matter is withdrawn in response to Applicant's amendment and arguments on p. 17.

Claim Rejections/Objections Maintained

In view of the amendment filed on 3/1/10, the following rejections are maintained.

Claim Objections

4. Claim 55 is objected to because of the following informalities: the recitation "the human IL-21 polypeptide comprises SEQ ID NO:2" is not for a protein molecule because "a polypeptide comprising SEQ ID NO:2" only contains the text "SEQ ID NO:2". It should be "the human IL-21 polypeptide comprises the amino acid sequence of SEQ ID NO:2" Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 5-15, 19, 29-35, 51-52, 54-57 and 59-74 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for increasing production of IL-10 and decreasing INF-γ ,IL-1α, IL-2, IL-6, IL-18 and increasing T cell proliferation in an EAE animal model by administration of the IL-21 polypeptide of SEQ ID NO:2 to decrease the severity of symptoms in MS that are regulated by inappropriate cytokine production, does not reasonably provide enablement for decreasing an INF-γ parameter of a subject having an undefined excess of INF-γ or for increasing an IL-10 parameter of a subject having an undefined IL-10 deficiency by administering to the subject an agonist of an IL-21/IL-21R as recited in claims 1, 29, 34 and 35 as broadly claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

make and use the invention commensurate in scope with these claims. The rejection is maintained for the reasons made of record and the reasons set forth below.

Claims 1, 5-15, 19, 29-35, 51-52, 54-57 and 59-74 as amended are drawn to a method of decreasing an INF-γ parameter of a subject having an excess of INF-γ and a method of increasing an IL-10 parameter of a subject having an IL-10 deficiency by administering to the subject an agonist of an IL-21/IL-21R wherein the agonist is selected from the group consisting of a human IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO: 2 or 4 or an agonistic anti-human/mouse IL-21R antibody or antigen binding fragment binding to an IL-21R comprising an amino acid sequence at least about 95% to the amino acid sequence of SEQ ID NO: 6 or 8.

On p. 13 of the response, Applicant argues that no undue experimentation is required because the specification identifies possible "parameters" and defines the parameter as "qualitative or quantitative information about IL-10 levels or activity e.g., IL-10 mRNA, protein levels or activity" and corresponding IFN-γ on p. 5, paragraph [0014]. On p. 14 of the response, Applicant argues that a skilled artisan would know who has an excess of IFN-γ because the specification teaches the subject recited in the claims is to be contrasted with a normal subject on p. 5, paragraph [0014], p. 8, paragraph [0025] and p. 44, paragraph [0149] and the concept of normal in reference to at least one disease, multiple sclerosis, on p. 36-37, paragraph [0128]. On p. 14 of

the response, Applicant argues that independent claims have been amended to recite such parameters (levels of mRNA and protein and activity of protein) and one condition (multiple sclerosis).

Applicant's arguments with regard to the definition of parameter have been fully considered and they are persuasive. However, Applicant's arguments with regard to how to determine who has an excess of IFN-γ have been fully considered but they are not persuasive. Note that the levels of IFN-g or IL-10 in each individual or patient are different. Although a skilled artisan can measure the levels of IFN-g/IL-10 mRNA and protein as compared to controls, the instnat specification fails to teach which subject has an excess of IFN-γ when compared to controls and thus can be treated in the claimed method. In particular, the specification fails to teach what level or activity would be considered as "a substantial increase" and thus to dinstinguish which specific subject has an excess of IFN-γ or defeciency of IL-10 and thus need to or can be treated in the claimed method. In addition, with regard to the activity of proteins, the specification only describes examples to assay or evaluate an IL-10 activity but fails to limit what other specific number or parameters and activity of IL-10 and IFN-γ are and thus would be within the scope of the claims to evaluate and determine the effects in the claimed method. Thus, a skilled artisan would not readily know what specific values or parameters and activity of IL-10 and IFN-γ are and thus would be used to evaluate and determine the effects as in the claimed method. Accordingly, the rejection of claims 1, 5-15, 19, 29-35, 51-52, 54-57 and 59-74 under 35 U.S.C. 112, first paragraph, because

the specification does not enable the claimed invention commensurate in scope with the claims is maintained.

New Grounds of Rejection Necessitated by the Amendment

The following rejections are new grounds of rejections necessitated by the amendment filed on 3/1/10.

Claim Rejections - 35 USC § 112

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 5-15, 19, 29-35, 51-52, 54-57 and 59-74 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 5-15, 19, 29-35, 51-52, 54-57 and 59-74 as amended are drawn to a method of decreasing an INF-γ parameter of a subject having an excess of INF-γ and a method of increasing an IL-10 parameter of a subject having an IL-10 deficiency by administering to the subject an agonist of an IL-21/IL-21R wherein the agonist is selected from the group consisting of a human IL-21 polypeptide comprising an amino acid sequence at least about 95% identical to the amino acid sequence of SEQ ID NO: 2 or 4 or an agonistic anti-human/mouse IL-21R antibody or antigen binding fragment binding to an IL-21R comprising an amino acid sequence at least about 95% to the amino acid sequence of SEQ ID NO: 6 or 8.

Claims 1, 5-15, 19, 29-35, 51-52, 54-57 and 59-74 are indefinite because Applicant recites "at least about 95%" in claims 1, 5, 9, 29, 30, 34, 35, 54, 59, and 63. The rest of claims are indefinite as depending from indefinite claims. The recitation of "at least" in the claims implies a lower limit but this is in conflict with the recitation "about", which implies that there is no set lower limit. Thus, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention; and thus the claims are indefinite.

Conclusion

7. NO CLAIM IS ALLOWED.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Papers relating to this application may be submitted to Technology Center 1600, Group 1649 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chang-Yu Wang whose telephone number is (571) 272-4521. The examiner can normally be reached on Monday-Thursday from 8:30 AM to 6:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Stucker, can be reached at (571) 272-0911.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/CYW/
Chang-Yu Wang, Ph.D.
May 25, 2010

/Christine J Saoud/
Primary Examiner, Art Unit 1647